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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/722,357 | 11/24/2003 | Michela Gallagher | JHUC-0008-101 | 4705 |

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| EXAMINER | |
|---|---|
| RAE, CHARLESWORTH E | |

| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/722,357 | GALLAGHER ET AL. | |
| | Examiner | Art Unit | |
| | CHARLESWORTH RAE | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *01 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *44 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, filed 04/01/09, has been fully considered and made of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is final.

**Status of the Claims**

Claims 44 and 53 are currently pending in this application and are the subject of the Office action.

**REJECTION**

**Claim rejections – 35 USC 103(a)**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 44 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohuchida et al. (U.S. Patent No. 7,176,240), in view Sramek et al. (Sramek et al. The status of ongoing trials for mild cognitive impairment. Opin. Invest. Drugs. 2001;10(4):741-752).**

Claim 44 recites "a method of treating Mild Cognitive Impairment (MCI) in a mammal, comprising the step of administering a pharmaceutical composition comprising a therapeutically effective amount of a compound" having the below formula:

II

to said mammal, wherein:

X is -OH, -O-alkali metal, $-NH_2$, or –SH, and

R is $-CH[(CH_2)_xCH_3]_2$.

Claim 53 recites "wherein said mammal is human."

Ohuchida et al. teach a method for treating neurodegenerative diseases (e.g. Alzheimer's disease, Amyotropic lateral sclerosis, progressive supra nuclear palsy, oive-pontyo-cerebellar atrophy, multiple sclerosis, and AIDS dementia) comprising administering an effective amount of a pentanoic acid derivatives (e.g. valproic acid = applicant's elected compound species) in amounts useful for improvement of cerebral function in animals, including human beings (see abstract; col. 1, line 16 to col. 4, line 67; and col. 27, line 64 to col. 28, line 10). In particular, Ohuchida et al. (US Patent 7,176,240 B2) teach that pentanoic acid derivatives are potentially useful in improving the GABA receptor responses (column 3, lines 53-61; columns 7-8). Ohuchida et al. also teach that these pentanoic acid derivatives and non-toxic salts and acid addition salts thereof are useful for prevention and/or treatment for neurodegenerative disease (Alzheimer's disease etc.) and neuronal dysfunction by stroke or traumatic injury (multiple sclerosis etc.) (abstract). Ohuchida et al. disclose that abnormalities in the astrocyte may be the determinant factors in inducing various brain-related diseases (column 2, lines 17-19).

Although Ohuchida et al. provide a general teaching of neurodegenerative diseases, this reference does not teach MCI.

Sramek et al. is added to show that drugs that are employed to treat Alzheimer's disease (i.e. neurodegenerative diseases) are also likely to be used in the treatment of MCI. Sramek et al. teach that as much as 38% of the elderly population meet the criteria for MCI and that up to 15% of these patients (i.e. MCI patients) convert to Alzheimer's disease (AD) annually (abstract). Sramek et al. teach that since there is a

high conversion rate from MCI to AD, it is likely that many patients with MCI have underlying neuropathology of AD, and that treatment strategies developed for treating AD have been the first employed to treat patients with MCI (abstract).

It would have been obvious to a person of skill in the art at the time the invention was made to treat a patient with MCI as taught by Sramek et al. with a pentanoic acid derivative (e.g. valproic acid) as taught by Ouchida et al. to improve cerebral function. One would have been motivated to treat MCI with a pentanoic acid derivative (e.g. valproic acid) because Sramek et al. suggest that drugs used to treat AD may be used to treat MCI and Ouchida et al. teach pentanoic acid derivative drugs (e.g. valproic acid) for use in the treatment of AD. One would have expected to successfully treat MCI with a pentanoic acid derivative (e.g. valproic acid) because Ouchida et al. provides a general teaching for treating neurodegenerative diseases comprising administering an effective amount of a composition comprising a pentanoic acid derivative (e.g. valproic acid) and MCI is a neurodegenerative disease.

Thus, a person of skill in the art at the time the invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

**Response to applicant's arguments**

In response to applicant's argument that the combination of cited references is based on hindsight, it is noted that Sramek et al. teach that as much as 38% of the elderly population meet the criteria for MCI and that up to 15% of these patients (i.e. MCI patients) convert to Alzheimer's disease (AD) annually (abstract). Hence, a nexus

exist between AD and MCI. Further, Ouchida et al. provides a general teaching for treating neurodegenerative diseases comprising administering an effective amount of a composition comprising a pentanoic acid derivative (e.g. valproic acid; abstract; col. 1, line 16 to col. 4, line 67; and col. 27, line 64 to col. 28, line 10) and MCI is a neurodegenerative disease as evidenced by the teaching of Sramek et al. (abstract). Thus, applicant's argument that the combination of cited references is based on hindsight is not found to be persuasive because one of skill in the art at the time the invention was made would have been motivated to combine the cited references in view of the nexus between MCI and other neurodegenerative diseases (e.g. MCI).

In response to applicant's argument that one would not have reasonably expected that valproic acid would be effective to treat MCI, it is noted that Sramek et al. suggest that treatment strategies developed for treating AD have been the first employed to treat patients with MCI (abstract). In view of the nexus between AD and MCI as discussed above, it is the examine's position that one would reasonably expect to successfully treat a patient with MIC with a pentanoic acid derivative (e.g. valproic acid) in view of the fact that Sramek et al. teach that as much as 38% of the elderly population meet the criteria for MCI and that up to 15% of these patients (i.e. MCI patients) convert to Alzheimer's disease (AD) annually (abstract) and Ohuchida et al. teach that pentanoic acid derivatives are useful for prevention and/or treatment for neurodegenerative diseases. Besides, there is a paucity of effective treatments available to treat neurodegenerative diseases such that one would reasonably expect to successfully attempt to use a drug that is known to be effective to treat a particular

neurodegenerative disease (e.g. AD) to treat other neurodegenerative diseases (e.g. MCI) and both AD and MCI are neurodegenerative diseases absent objective evidence to the contrary (MPEP 2141; see also *KSR*, 550 U.S. at ___, 82 USPQ2d at 1391. Specifically, the Supreme Court stated that the Federal Circuit had erred in four ways: (1) "by holding that courts and patent examiners should look only to the problem the patentee was trying to solve " (*Id.* at ___, 82 USPQ2d at 1397); (2) by assuming "that a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem" (*Id.*); (3) by concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try'" (*Id.*); and (4) by overemphasizing "the risk of courts and patent examiners falling prey to hindsight bias" and as a result applying "[r]igid preventative rules that deny factfinders recourse to common sense" (*Id.* ).).

In addition, applicant's evidentiary reference (Exhibit A) is directed to method of treating MCI comprising a COX-2 inhibitor (RofecoxIb); Exhibit B is directed to a method of treating MCI with vitamin E, or donepezil, or placebo; and Exhibit C discloses that it is important to note that the present approach for MCI could be logically extended to other neurodegenerative disorders (page 195, last para.). Since valprioc acid does not share a common structure or mechanism of action with Rofecoxib (Exhibit A) or vitamin E (Exhibit B), one would not reasonably expect to extrapolate the study results disclosed in said exhibits to valproic acid. Hence, it is the examiner's position that Exhibits A, B, and C do not provide reasonable support for applicant's above arguments evidenced by the fact that Exhibit C discloses that it is important to note that the present approach for

MCI could be logically extended to other neurodegenerative disorders (page 195, last para.).

**Conclusion**

**THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

26 June 2009
/C. R./ Examiner, Art Unit 1611

**/Sharmila Gollamudi Landau/**

**Supervisory Patent Examiner, Art Unit 1611**